

CLAIMS

1. A method of repressing, delaying or otherwise reducing the expression of a target gene in an animal cell, tissue or organ, said method comprising introducing to said animal cell, tissue or organ one or more dispersed nucleic acid molecules or foreign nucleic acid molecules comprising tandem copies of a nucleotide sequence which is substantially identical to the nucleotide sequence of said target gene or a region thereof or complementary thereto for a time and under conditions sufficient for translation of the mRNA product of said target gene to be modified, subject to the proviso that the transcription of said mRNA product is not exclusively repressed or reduced.
2. The method according to claim 1 wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise inverted repeats of the target gene sequence or a region thereof or complementary thereto.
3. The method according to claim 1 wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise direct repeats of the target gene sequence or a region thereof or complementary thereto.
4. The method according to claim 1 wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise both direct and inverted repeats of the target gene sequence or a region thereof or complementary thereto.
5. The method according to any one of claims 1 to 4, wherein the number of copies of the target gene sequence or region thereof or complementary thereto in the dispersed nucleic acid molecule or foreign nucleic acid molecule is two.
6. The method according to any one of claims 1 to 4, wherein the number of copies of the target gene sequence or region thereof or complementary thereto in the dispersed nucleic acid molecule or foreign nucleic acid molecule is three.

- 75 -

7. The method according to any one of claims 1 to 4, wherein the number of copies of the target gene sequence or region thereof or complementary thereto in the dispersed nucleic acid molecule or foreign nucleic acid molecule is four.
8. The method according to any one of claims 1 to 4, wherein the number of copies of the target gene sequence or region thereof or complementary thereto in the dispersed nucleic acid molecule or foreign nucleic acid molecule is six.
9. The method according to any one of claims 1 to 4, wherein the number of copies of the target gene sequence or region thereof or complementary thereto in the dispersed nucleic acid molecule or foreign nucleic acid molecule is ten.
10. The method according to any one of claims one to 9 wherein the dispersed nucleic acid molecule or foreign nucleic acid molecule comprises tandem repeats of the target gene sequence and wherein one or more of the repeated units of said tandem repeats is separated from another unit by a nucleic acid-containing stuffer fragment.
11. The method according to claim 1 wherein the animal is a mouse.
12. The method according to any one of claims 1 to 11 wherein the target gene is a gene which is contained within the genome of the animal cell, tissue or organ.
13. The method according to claim 12 wherein the target gene is α -1,3-galactosyltransferase.
14. The method according to any one of claims 1 to 13 wherein the target gene is derived from the genome of a pathogen of the animal cell, tissue or organ or an organism comprising said cell, tissue or organ.
15. The method according to claim 14 wherein the pathogen is a virus.

- 76 -

16. The method according to claim 15 wherein the virus is BEV.
17. The method according to any one of claims 1 to 16 further comprising selecting the dispersed nucleic acid molecule(s) or foreign nucleic acid molecule(s) according to their ability to effectively modulate expression of the target gene.
18. A method of repressing, delaying or otherwise reducing the expression of a target gene in an animal cell, tissue or organ, said method comprising:
 - (i) selecting one or more dispersed nucleic acid molecules or foreign nucleic acid molecules which comprise tandem repeats of a nucleotide sequence which is substantially identical to the nucleotide sequence of said target gene or a region thereof or which is complementary thereto;
 - (ii) producing a synthetic gene comprising said dispersed nucleic acid molecules or foreign nucleic acid molecules operably connected to a promoter sequence operable in said animal cell, tissue or organ;
 - (iii) introducing said synthetic gene to said cell, tissue or organ; and
 - (iv) expressing said synthetic gene in said cell, tissue or organ for a time and under conditions sufficient for translation of the mRNA product of said target gene to be modified, subject to the proviso that the transcription of said mRNA product is not exclusively repressed or reduced.
19. A method of conferring resistance or immunity to a viral pathogen upon an animal cell, tissue, organ or whole organism, comprising introducing one or more dispersed nucleic acid molecules or foreign nucleic acid molecules which comprise tandem repeats of a nucleotide sequence derived from the viral pathogen or a complementary sequence thereto for a time and under conditions sufficient for translation of the mRNA product of a virus gene to be delayed or otherwise reduced, subject to the proviso that the transcription of said mRNA product is not exclusively

- 77 -

repressed or reduced.

20. The method according to claim 19 wherein the virus is an animal pathogen.
21. The method according to claim 20 wherein the virus is BEV.
22. The method according to any one of claims 19 to 21 further comprising selecting the dispersed nucleic acid molecule(s) or foreign nucleic acid molecule(s) according to their ability to confer resistance or immunity on the animal cell, tissue, organ or organism.
23. A method of conferring resistance or immunity to a viral pathogen upon an animal cell, tissue, organ or whole organism, comprising:
 - (i) selecting one or more dispersed nucleic acid molecules or foreign nucleic acid molecules which comprise tandem repeats of a nucleotide sequence derived from the viral pathogen or a complementary sequence thereto;
 - (ii) producing a synthetic gene comprising said dispersed nucleic acid molecules or foreign nucleic acid molecules operably connected to a promoter sequence operable in said cell, tissue, organ or whole organism;
 - (iii) introducing said synthetic gene to said cell, tissue, organ or whole organism; and
 - (iv) expressing said synthetic gene in said cell, tissue or organ for a time and under conditions sufficient for translation of the mRNA product of a gene of the virus to be modified, subject to the proviso that the transcription of said mRNA product is not exclusively repressed or reduced.

- 78 -

24. The method according to any one of claims 19 to 23, wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise tandem copies of nucleotide sequence encoding a viral replicase, polymerase, coat protein or uncoating gene.
25. The method according to claim 24 wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise tandem copies of nucleotide sequence encoding a viral polymerase.
26. The method according to claim 25 wherein the dispersed nucleic acid molecules or foreign nucleic acid molecules comprise tandem copies of nucleotide sequence encoding a viral coat protein.
27. A synthetic gene when used in accordance with the method of claim 1 to repress, delay or otherwise reduce the expression of a target gene in an animal cell, tissue, organ or whole organism, wherein said synthetic gene comprises a dispersed nucleic acid molecule or a foreign nucleic acid molecule comprising tandem copies of a nucleotide sequence which is substantially identical to the nucleotide sequence of said target gene or a derivative thereof or a complementary sequence thereto placed operably under the control of a promoter sequence which is operable in said animal cell, tissue, organ or whole organism.
28. The synthetic gene according to claim 27, wherein the dispersed nucleic acid molecule or a foreign nucleic acid molecule comprises tandem inverted and/or direct repeats of a genetic sequence that is endogenous to the genome of the animal cell, tissue, organ or organism or which is derived from a non-endogenous gene of the animal cell, tissue, organ or organism.
29. The synthetic gene according to claim 28 wherein the non-endogenous gene is derived from a viral pathogen of the animal cell, tissue, organ or organism.
30. The synthetic gene according to claim 29 wherein the non-endogenous gene

is derived from an animal virus.

31. The synthetic gene according to claim 30 wherein the animal virus is BEV.
32. The synthetic gene according to claim 30 wherein the non-endogenous gene is derived from the BEV polymerase gene.
33. The synthetic gene according to claim 32 wherein the promoter is the CMV-IE promoter or SV40 promoter sequence.
34. The synthetic gene according to claims 27 or 28 wherein the dispersed nucleic acid molecule or a foreign nucleic acid molecule comprises tandem inverted and/or direct repeats of the porcine α -1,3-galactosyltransferase gene.
35. The synthetic gene according to claim 24 wherein the porcine α -1,3-galactosyltransferase gene is placed operably in connection with the CMV promoter sequence.
36. The synthetic gene according to any one of claims 27 to 35 wherein the tandem copies of the nucleotide sequence of the target gene are operably connected to two or more promoter sequences.
37. The synthetic gene according to claim 36 wherein each of the tandem copies of the nucleotide sequence of the target gene are operably connected to spatially separate promoter sequences.
38. A genetic construct comprising the synthetic gene according to any one of claims 27 to 37.
39. The genetic construct according to claim 38 selected from the list comprising plasmid pCMV.BEVx2; plasmid pCMV.BEV.GFP.VEB; plasmid pCMV.BEV.SV40L.BEV; and plasmid pCMV.BEV.SV40L.VEB.

- 80 -

40. The genetic construct according to claim 38 selected from plasmid pCMV.Galtx2; and pCMV.Galtx4.
41. Use of the genetic construct according to claim 39 to confer immunity or resistance against BEV upon an animal cell, tissue or organ or a whole animal.
42. Use of the genetic construct according to claim 40 to delay, repress or otherwise reduce expression of α -1,3-galactosyltransferase in an animal cell, tissue, organ or whole organism that would otherwise express same.
43. An animal cell, tissue, organ or whole organism comprising the synthetic gene according to any one of claims 27 to 37 or the genetic construct according to any one of claims 38 to 40.